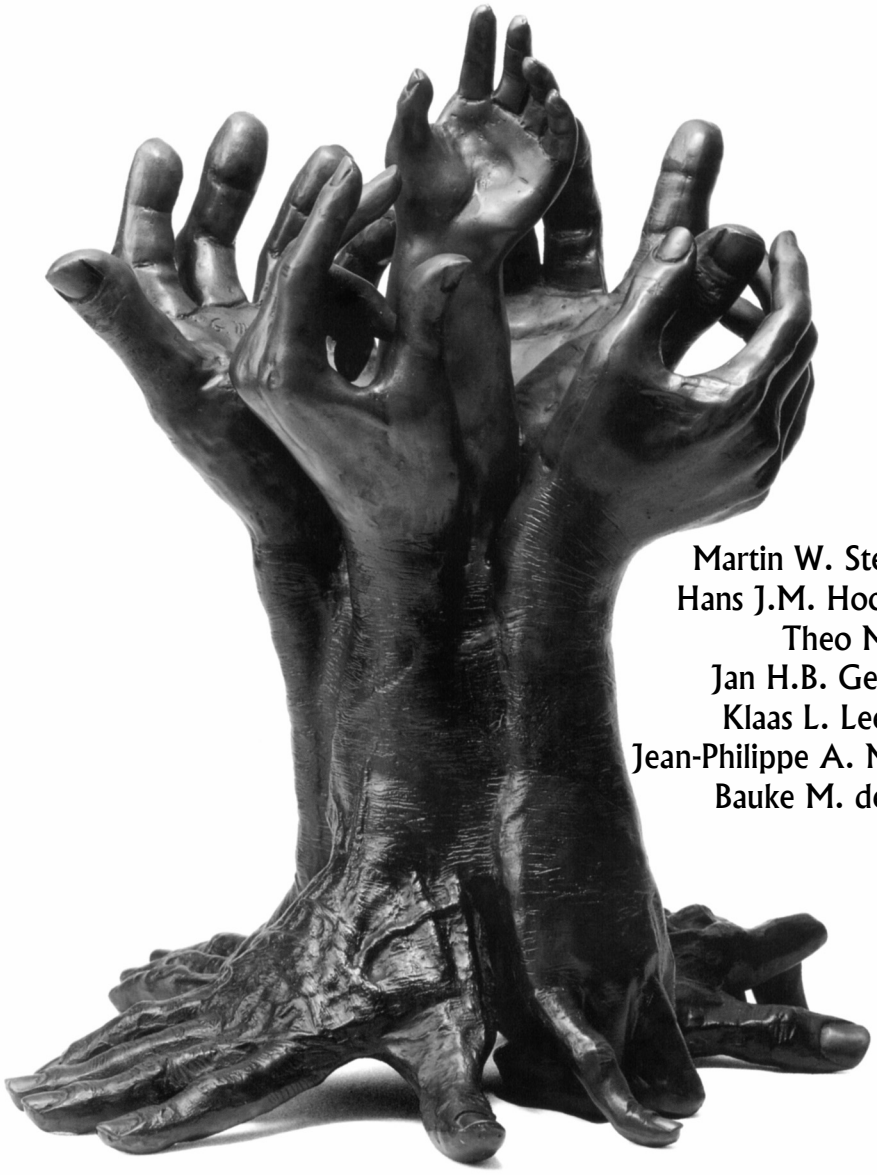
Cerebral reorganization and motor imagery after flexor tendon Repair

Stenekes, Martin Willian

Chapter 4

Functional dominance of finger flexion over extension, expressed in left parietal activation



Martin W. Stenekes
Hans J.M. Hoogduin
Theo Mulder
Jan H.B. Geertzen
Klaas L. Leenders
Jean-Philippe A. Nicolai
Bauke M. de Jong

NeuroImage 2006; 32: 676-683

Abstract

Sensory stimuli may elicit a widely distributed parietal-premotor circuitry underlying task-related movements such as grasping. These stimuli include the visual presentation of an object to be grasped, as well as the observation of grasping performed by others. In this study we used functional Magnetic Resonance Imaging (fMRI) to test whether the performance of simple finger flexion, contrasted to extension, might similarly activate higher-order circuitry associated with grasping. Statistical Parametric Mapping (SPM) showed that flexion, compared to extension, was related with significant activation of the left posterior parietal cortex and posterior insula, bilaterally. This pattern supported our hypothesis that simple finger flexion has a specific relation with circuitry involved in preparing manual tasks. Although the two motor conditions showed major overlap in the primary motor cortex, increased flexion-related activation at the precentral motor-premotor junction further supported its association with higher order-motor control.

Introduction

Grasping movements provide the ability to manipulate objects in surrounding space. This implies tuning of finger positions to the shape of an object being reached for. The cerebral organisation of such visuomotor function is embedded in circuitry distributed over parietal and premotor cortical regions without a strict regional demarcation between perceptual and motor representations[1-3]. Both premotor and parietal cortical regions have been involved in grasping an object as well as observing this object. These action-associated networks can further be activated, in a mirror fashion, by action observation[4], action sounds[5] or the verbal description of action[6], thus demonstrating that stimulation by specific perceptual fragments provides access to circuitry underlying higher-order motor control[7]. This raises the question whether the performance of a simple motor act without a specified goal or object to grasp, might similarly activate such circuitry.

Previously, we have shown that the left parietal 'grasping' region does not only contribute to the integration of object shape and hand posture. It is also active during hand posturing, independent of the shape of the target being reached for[8]. This command function was explained as being an active process of integrating body scheme information into the organisation of movement, which is consistent with clinical characteristics seen in apraxia[9]. In the present study, an important consideration was that in grasping the initial opening of the hand is less task-specific compared with subsequent finger flexion. Although indeed the initial grip aperture is guided by the spatial dimensions of the target, subsequent flexion provides the precision grip with both the exact adjustment of separate fingers to the shape of the target, and the coordination of fingertip forces[10;11]. One might thus infer that flexion is more involved in higher-order motor control than finger extension. We therefore hypothesized that simple flexion, contrasted to extension, is associated with activation in parietal and premotor cortex. In order to answer this question, functional brain imaging based on the detection of regional changes in relative perfusion was applied[12]. By using appropriate task conditions, this methodology allows the identification of cerebral structures that deal with aspects of the cerebral organisation of movement that lie beyond the primary motor cortex.

A second issue concerned the functional distribution of finger movements over the primary motor cortex. The somatotopic representation of body parts, including separate fingers, is well-established, although patterns of overlap exist[13-16]. The difference between flexion and extension of the same fingers, however, does not easily fit in this scheme. In analogy with the differences between proximal and distal sensory stimulation of the same finger[17], we particularly looked for

a functional segregation between deep and superficial segments of the anterior wall of the central sulcus.

Materials and Methods

Twelve healthy right-handed subjects (eight males, four females) were studied with functional Magnetic Resonance Imaging using a 3T Intera Philips MRI scanner (Best, The Netherlands) with a standard 6-channel SENSE head coil. The following pulse sequence parameters were used: FFE single shot EPI; 46 slices; slice thickness 3.5 mm; no gap; field of view 224 mm; scanning matrix 64x64; transverse slice orientation; repetition time (TR) = 3 s; echo time (TE) = 35 ms; flip angle 90°. Subjects gave informed consent to a protocol approved by the local Medical Ethics Committee. Their ages ranged from 20 to 63 years (median 29). None of the subjects had known neurological disorders or a history of upper extremity disorders. Before scanning, the tasks were explained and practiced shortly. Data were acquired in four subsequent sessions, of which each consisted of four 33-second movement blocks that were each preceded by a control block. In one block, 11 brain volumes of 46 slices were obtained. Beeps were presented by headphone at random intervals (1.5 to 4.5 s), in 33-second blocks. At the onset of each block, auditory instructions (by headphone) indicated the condition during that block, being either *Flexion*, *Extension* or *Rest*. Subjects had their eyes closed. The two movement conditions were scheduled in a balanced order.

The left arm was positioned with the volar side of the hand facing the floor. The forearm and wrist were supported by a pillow on the scanner table, while the fingers could move freely. In the flexion condition, subjects responded to each beep by two rapid flexion movements of the left-hand fingers, except for the thumb. The two successive flexion movements were each followed by relaxation, which enabled the fingers to passively regain their neutral position. In the extension condition, two extension movements of the same fingers (digits 2-5) were made, similarly followed by relaxation of the muscles. In the rest condition subjects only listened to the beeps, no motor responses were given. The execution of the movement tasks was recorded by a camera in the scanner room and monitored on a television-screen in the console room. Subjects were allowed to execute the strictly paced movements in a natural fashion. Although we thus refrained from explicitly controlling subtle variations in force, the advantage of this design was that the flexion and extension tasks were balanced for attentional demand.

The kinetic characteristics of performance during scanning were not quantified. However, observations confirmed that the movements resembled those that were demonstrated during the instructions before scanning. The instructed position of the relaxed hand implied that the

metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints were each held at an angle of about 45° deviating from the virtual axis along a fully extended joint (Fig. 4.1). Active flexion was mainly accomplished by movements in these two joints: the angle in the MCP-joint increased by 15° to 60°, while the angle in the PIP-joint increased by 35° to 80°. The fingertips did not touch the palm. During extension, the angles in these two joints decreased by approximately 35° each, resulting in almost straight fingers. The occurrence of consistent relaxation between two brisk successive movements in this task was previously documented by surface electromyography in normal circumstances[18]. Only in pathological conditions did such relaxation fail. The reason to employ a left-hand movement paradigm in the present study was to maintain similarity with the protocol used in our previous left-hand tendon lesion study.

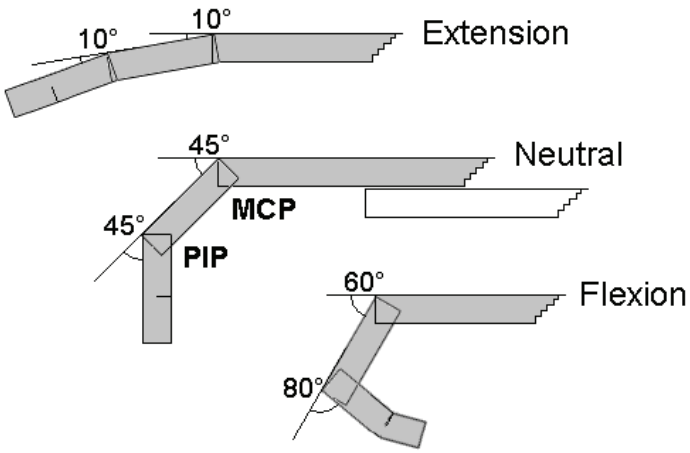


Figure 4.1 Schematic illustration of the instructed hand movements. The forearm and wrist were supported. In the flexion condition, subjects responded to each single beep by two brisk flexion movements of the left-hand fingers, except for the thumb. The two successive flexion movements were each followed by relaxation, which enabled the fingers to passively regain their neutral position. In the extension condition, two extension movements of the same fingers (digits 2-5) were made, similarly followed by relaxation of the muscles. MCP = metacarpophalangeal joint; PIP = proximal interphalangeal joint.

Image processing and statistical analysis were conducted with Statistical Parametric mapping[19] (version SPM2, Wellcome Department of Neuroimaging, London, UK; www.fil.ion.ucl.ac.uk/spm). Pre-processing included realignment of all images to the first one, and subsequent spatial normalization onto a standard brain template (Montreal Neurological Institute, MNI template in SPM). For whole brain analysis, images were smoothed with a

Gaussian filter of 10 mm FWHM. In addition, the images were smoothed with a 4 mm filter as to detect differences in activation in the primary motor cortex. The movement conditions were contrasted both to rest and to each other. The group results were obtained by fixed-effects analysis (Fig. 4.2).

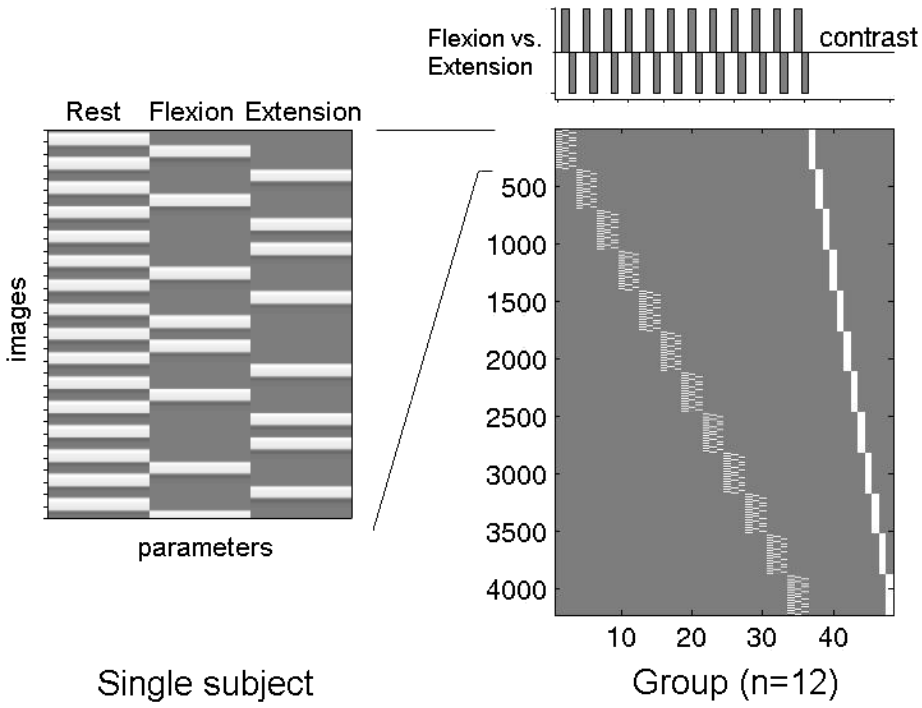


Figure 4.2 Design matrix of the applied fixed-effect analysis by SPM, illustrating the contrast of increased BOLD responses related to flexion (+1) versus extension (-1), with the non-motor (rest) condition set to zero. For each subject, a total of 8 flexion- and 8 extension blocks were ordered in pairs [Flex. Ext.] and [Ext. Flex.], while each movement block was preceded by a rest block. A single condition block consists of 11 measurements of a whole brain volume, which implies that 352 volumes (images) were acquired from each of the 12 subjects.

Results

Subjects had no difficulty performing the tasks correctly as could be visually examined on the television. They did not experience one of the two tasks more difficult than the other one. The two movement conditions, compared to rest, showed common activation in predominantly the contralateral sensorimotor cortex, ipsilateral cerebellum and supplementary motor area (SMA)

(Fig. 4.3, see Appendix, Table 4.1). Group analysis of changes in BOLD response (10 mm filter initial threshold for response-height at voxel-level $p = 0.001$) revealed that finger flexion, when contrasted to extension, was related to significant activation in the ipsilateral (left) parietal cortex ($p < 0.05$, cluster-level corrected for whole brain volume) (Fig. 4.4, see Appendix, Table 4.2). This focus of activation was found at a postero-superior location along the intra-parietal sulcus. In addition, significant activations were found in the posterior insula of both hemispheres (Fig. 4.4, see Appendix). Contrasting extension to flexion movement did not result in significant activation (at cluster-level). In Figure 4.5, the parietal effects of flexion and extension are plotted for each subject, illustrating that the group result was supported by all subjects.

Table 4.1 Movement-related activation

		Stereotactic coordinates (x, y z)							
		Left				**Right**			
Brain region	[BA]	x	y	z	Z-score	x	y	z	Z-score
SMA	[6]					4	0	56	>8
Sensori-motor cortex	[4]					40	-24	62	>8
						40	-14	62	>8
Prefrontal cortex	[45]/[46]					44	38	26	>8
Premotor cortex	[6]	-44	-2	58	>8	58	10	36	>8
		-60	10	30	>8	62	-14	44	>8
Anterior parietal Cortex	[40]	-64	-18	14	>8	66	-26	18	>8
		-48	-42	56	>8	62	-26	36	>8
Putamen						30	-8	-4	>8
Operculum/Insula	[38]/[48]	-52	8	-8	>8	54	8	-8	>8
Thalamus		-8	-18	8	>8	10	-18	6	>8

Coordinates of the activation regions related to left-hand movement, i.e. both flexion and extension contrasted to rest (group of 12 subjects, $p < 0.01$, family-wise error-correction for the whole brain volume). Spatial smoothing filter was 10 mm. Positive x,y,z coordinates (in mm) indicate locations on respectively the right of, anterior and superior to the middle of the anterior commissure.
BA = Brodmann's Area.

Table 4.2 Flexion-related activation (whole brain)

		Stereotactic coordinates (x, y z)									
		Left					Right				
Brain region	[BA]	x	y	z	Z-score	kE	x	y	z	Z-score	kE
Parietal cortex	[40]	-32	-60	56	4.0	620					
Posterior insula	[48]	-36	-22	-2	4.4	581	38	-4	14	5.4	430

Coordinates of the activation maxima related to left-hand finger flexion contrasted to extension (group analysis, $p < 0.05$, cluster-level corrected for whole brain volume). kE = extent of the cluster, expressed by the number of voxels. Spatial smoothing filter was 10 mm. Extension contrasted to flexion did not reveal significant activation with this threshold. Conventions are as in Table 4.1.

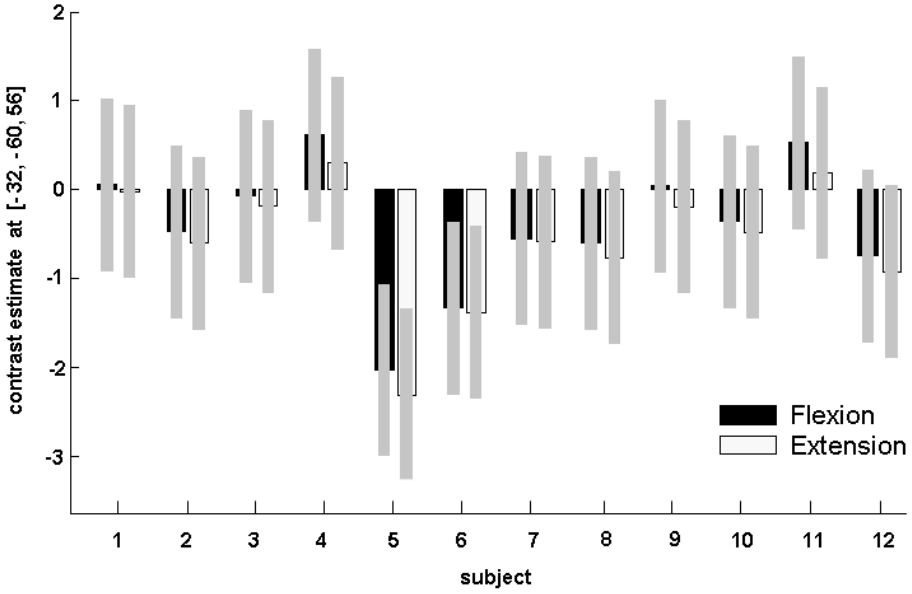


Figure 4.5 Contrast estimates (and 90% confidence intervals, c.i.) with the effects of flexion and extension in the left parietal cortex for each of the 12 subjects. The estimates were derived from the focus of maximum activation at [x –32, y –60, z 56], identified by the group analysis. Seven subjects showed a cluster of robust activation, while in the other 5 subjects, activations were smaller. In the individual subjects the local maximum of parietal activation might be at a slightly different location as the group maximum.

Our second question concerned the possible segregation between the representation of finger flexion and extension in the motor cortex. At relaxed statistical threshold, and using the 4 mm filter, again overlap in the contralateral sensorimotor cortex was the most prominent

observation. However, subtle differences could be noticed. Activation resulting from finger flexion, compared to rest, extended more lateral to the cerebral convexity than the extension-related activation (Fig. 4.6a,c, see Appendix; Table 4.3). Moreover, activation related to extension, when contrasted to flexion, was found deep in the central sulcus ($p < 0.05$, at voxel-level, uncorrected), whereas finger flexion, contrasted to extension revealed activation more laterally in the motor cortex, reaching the surface of the pre-central gyrus (Fig. 4.6b,d, see Appendix). At this lateral location, the primary motor cortex (Brodmann's Area, BA4) borders on the premotor cortex BA 6. In addition, the latter contrast (flexion vs. extension) showed activation of the primary sensory cortex at the post-central gyrus. The extension-specific activation in the fundus of the central sulcus (Fig. 4.6d, see Appendix) was near the junction between BA 4 and sensory cortex BA 3. Although an unequivocal distinction is difficult to make, the slight spread in the precentral gyrus, observed in adjacent superior slices (see also Table 4.3), supports involvement of the primary motor cortex (BA 4).

Table 4.3 Segregation along the central sulcus

	Stereotactic coordinates (x, y z)							
	Left				**Right**			
Contrast	x	y	z	Z-score	x	y	z	Z-score
Flexion versus rest					36	-22	54	>8
					42	-26	62	>8
Flexion versus extension					50	-22	54	6.0
Extension versus rest					36	-22	54	>8
					38	-34	68	>8
Extension versus flexion					26	-22	56	2.9
					28	-24	64	2.7

Coordinates of the activation maxima of the contralateral motor cortex related to left-hand finger flexion contrasted to extension, and finger extension contrasted to flexion ($p < 0.05$, voxel-level, uncorrected). Spatial smoothing filter was 4 mm. Conventions are as in Table 4.1.

Discussion

The distribution of flexion-related activation demonstrated that, unlike extension, finger flexion has a strong relation with higher-order motor control. This supported our hypothesis. Particularly the left parietal activation, ipsilateral to the executed movements, represents a

crucial node in a network subserving adequate manipulation of objects[20]. At different levels, the posterior parietal cortex has been associated with the organisation of task-related movement, ranging from intention, prehension to actual visuomotor- and somatosensorimotor integration[2;11;21-24]. The fact that we found the parietal activation in the left hemisphere, ipsilateral to the moving hand, points at a specific left (dominant) hemisphere function. The contribution of body scheme to prehensile command is such a lateralized function for the parietal cortex[8], of which deficit results in ideomotor apraxia[9;20]. The ipsilateral location is a strong argument against the view that the parietal activation was the result of possible increased proprioceptive feedback in finger flexion. The supporting role of the posterior insula in skeletomotor control has been established in both human and other primates, although its specific contribution has not been fully elucidated yet[25-27].

The recruitment of distributed circuitry by simple flexion movement was consistent with our assumption that particularly finger flexion is a motor act which is functionally implicated in complex movement such as grasping. This association may also be inferred from the cerebral effects of dynamic immobilization following flexor tendon surgery[28]. We have recently described that after a period of splinting with elastic strings, enabling only passive and not active flexion movement, clumsiness in task performance remained for weeks. Repeated functional brain imaging revealed that prolonged absence of active flexion movement had induced changes in the cerebral organisation of hand movement[18]. Recruitment of distributed action-related circuitry by sensory stimuli has been well described. A classical finding, in this respect, concerned the behavior of ventral premotor neurons, that were activated during both the observation of meaningful hand movement by others and the effective execution of such movement[29]. These neurons were consequently called mirror-neurons. Later, action observation appeared to induce activation of a wider distributed parietal-premotor network[4;30]. This enables observations to be matched onto the motor system[31]. Recent findings have shown that even indirect stimuli such as action sounds, may recruit the action-related circuitries[5]. This indicates that the now often coined ‘mirror-neuron system’ reflects a cerebral organisation that goes beyond mirror-mode processing. A general principle of cerebral processing might be that a distributed, functionally coherent, cerebral network is recruited by activation of one of its crucial nodes[32]. Along such nodes, network-access is allowed to a wide range of sensory stimuli. Our finding indicates that access can similarly be obtained by a motor act.

Although flexion and extension predominantly shared the focus of activation in the primary motor cortex, contrasting the two motor conditions revealed a segregation with the flexion-related activation extending to the motor-premotor junction on the precentral gyrus. Extension-

related activation, contrasted to flexion, was deep in the central sulcus. This distribution, particularly with the relation between flexion and premotor cortex activation, provides an additional argument for the strong association between finger flexion and task-related movement, which is indeed naturally expressed in grasping. Functional differentiation along the anterior wall of the central sulcus with a segregation between deep (posterior, BA 4p) and superficial (anterior, BA 4a) segments of the primary motor cortex has previously been described[33]. While subjects made the same stereotypic finger movements, they found that activation related to the instructed motor task remained high in the BA 4a, independent from visual distraction, while activation deep in the central sulcus (BA 4p) decreased in such condition. Modulation of activation in the latter was inferred to reflect modulation of attention to action. In addition, one might consider that the maintained high activation in BA 4a points at a strong anchoring of instructed, task-related movement. It is a challenging idea to assume that such anchoring is logically associated with input from the adjacent premotor cortex (BA 6)[34].

Finger flexion and extension movements are executed by the same body parts. On the other hand, these movements are functionally distinct and made by different muscles. Similar conceptual considerations have been made with regard to the difference between the motor representation of separate fingers versus the representation of separate hand muscles. Although gradients of segregated finger representations remain a repeatedly confirmed finding, overlap of these representations, as well as distributed multifocal representation, has been emphasized[13;14;35]. In brain activation studies, the somatotopic representation of fingers on the motor cortex was enhanced by contrasting one finger to the others. The additional complexity of representation has been proposed to reflect the flexibility to achieve an indeed enormous repertoire of movements with the same fingers, based on specific combinations of muscle contractions[13;36]. In this respect, our finding of both overlap and segregation concerning two opposite movements of the same fingers is consistent with the findings concerning movement representations of different fingers.

The two movement conditions that were applied in our study were particularly characterized by the swift alternation of contraction and subsequent relaxation. These movements were made in a natural fashion, without a difference in perceived task difficulty. Although the two conditions were thus balanced for attentional demand, one might argue that in natural movement, finger flexion is more forceful than extension, thus introducing a possible bias between flexion and force. We regard this explanation unlikely. In the literature, modulation of force has particularly been associated with changing activations in sensorimotor cortex, SMA, cerebellum and basal ganglia[37;38], whereas in our study, flexion-specific activation was not in the center of the

movement-related activation, but at the border between the primary motor cortex and premotor cortex. One might oppose that, although the magnitude of activation in the centre did not differ between flexion and extension, possible greater force in flexion would include more widespread recruitment of muscles and an associated increase of proprioceptive feedback. This might thus result in a larger spread of sensorimotor cortex activation. In our study, however, we did not only see a lateral expansion of activation related to flexion, a small extension-specific spread was seen towards the fundus of the central sulcus. Additional arguments against the idea that differences in force might explain our results include the absence of flexion-specific activation in SMA, basal ganglia and cerebellum[37;38]. On the other hand, the posterior parietal cortex has recently been implicated in the co-ordination of fingertip forces[11]. In a previous study, Ehrsson et al.[39] already demonstrated the specific involvement of parietal- and premotor cortex in the production of force in precision grip, when contrasted to power grip. This context-dependent effect of force supports our concept that simple movement qualities may be intrinsically related to higher-order motor.

To conclude, finger flexion, more than extension, may be regarded as a basic element in the organisation of complex movements such as grasping. We thus infer that specific simple motor acts may recruit a cerebral network implicated in the organisation of more complex action. This suggests an analogy with the activation of an action supporting cerebral network by specific sensory stimuli. Finally, we found indications that antagonist muscle groups of the same fingers can be somatotopically distinguished on the motor cortex.

References

1. Sakata H, Taira M, Murata A, Mine S. Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. *Cereb. Cortex* 1995; 5: 429-38.

2. Wise SP, Boussaoud D, Johnson PB, Caminiti R. Premotor and parietal cortex: corticocortical connectivity and combinatorial computations. *Annu. Rev. Neurosci.* 1997; 20: 25-42.

3. Goodale MA. Visuomotor control: where does vision end and action begin? *Curr. Biol.* 1998; 8: R489-R491.

4. Buccino G, Binkofski F, Fink GR *et al*. Action observation activates premotor and parietal areas in a somatotopic manner: an fMRI study. *Eur. J. Neurosci.* 2001; 13: 400-4.

5. Kohler E, Keysers C, Umilta MA *et al*. Hearing sounds, understanding actions: action representation in mirror neurons. *Science* 2002; 297: 846-8.

6. Tettamanti M, Buccino G, Saccuman MC *et al*. Listening to action-related sentences activates fronto-parietal motor circuits. *J.Cogn. Neurosci.* 2005; 17: 273-81.

7. Georgopoulos AP. Higher order motor control. *Annu. Rev. Neurosci.* 1991; 14: 361-77.

8. de Jong BM, van der Graaf FH, Paans AM. Brain activation related to the representations of external space and body scheme in visuomotor control. *Neuroimage* 2001; 14: 1128-35.

9. Poizner H, Clark MA, Merians AS *et al*. Joint coordination deficits in limb apraxia. *Brain* 1995; 118: 227-42.

10. Castiello U. The neuroscience of grasping. *Nat. Rev. Neurosci.* 2005; 6: 726-36.

11. Ehrsson HH, Fagergren A, Johansson RS, Forssberg H. Evidence for the involvement of the posterior parietal cortex in coordination of fingertip forces for grasp stability in manipulation. *J. Neurophysiol.* 2003; 90: 2978-86.

12. Raichle ME. Behind the scenes of functional brain imaging: a historical and physiological perspective. *Proc. Natl. Acad. Sci. U.S.A.* 1998; 95: 765-72.

13. Dechent P,.Frahm J. Functional somatotopy of finger representations in human primary motor cortex. *Hum. Brain Mapp.* 2003; 18: 272-83.

14. Hlustik P, Solodkin A, Gullapalli RP, Noll DC, Small SL. Somatotopy in human primary motor and somatosensory hand representations revisited. *Cereb. Cortex* 2001; 11: 312-21.

15. Kaas JH, Nelson RJ, Sur M, Lin CS, Merzenich MM. Multiple representations of the body within the primary somatosensory cortex of primates. *Science* 1979; 204: 521-3.

16. Penfield W, Rasmussen T. The cerebral cortex of man: a clinical study of localization of function. New York: Macmillan, 1950.

17. Blankenburg F, Ruben J, Meyer R, Schwiemann J, Villringer A. Evidence for a rostral-to-caudal somatotopic organization in human primary somatosensory cortex with mirror-reversal in areas 3b and 1. *Cereb. Cortex* 2003; 13: 987-93.

18. de Jong BM, Coert JH, Stenekes MW *et al*. Cerebral reorganisation of human hand movement following dynamic immobilisation. *Neuroreport* 2003; 14: 1693-6.

19. Friston KJ, Holmes AP, Worsley KJ *et al*. Statistical parametric maps in functional imaging: a general linear approach. *Hum. Brain Mapp.* 1994; 2: 189-210.

20. Heilman KM, Rothi LJG. Apraxia. *Clinical neuropsychology*, pp 131-50. New York: Oxford University Press, 1993.

21. Andersen RA,.Buneo CA. Intentional maps in posterior parietal cortex. *Annu. Rev. Neurosci.* 2002; 25: 189-220.

22. Binkofski F, Buccino G, Posse S *et al*. A fronto-parietal circuit for object manipulation in man: evidence from an fMRI-study. *Eur. J. Neurosci.* 1999; 11: 3276-86.

23. Jancke L, Kleinschmidt A, Mirzazade S, Shah NJ, Freund HJ. The role of the inferior parietal cortex in linking the tactile perception and manual construction of object shapes. *Cereb. Cortex* 2001; 11: 114-21.

24. Stoeckel MC, Weder B, Binkofski F *et al*. Left and right superior parietal lobule in tactile object discrimination. *Eur. J. Neurosci.* 2004; 19: 1067-72.

25. Mesulam MM, Mufson EJ. The insula of Reil in man and monkey. *Cerebral Cortex*, pp 179-226. New York: Plenum Press, 1985.

26. Weiller C, Chollet F, Friston KJ, Wise RJ, Frackowiak RS. Functional reorganization of the brain in recovery from striatocapsular infarction in man. *Ann. Neurol.* 1992; 31: 463-72.

27. Fink GR, Frackowiak RS, Pietrzyk U, Passingham RE. Multiple nonprimary motor areas in the human cortex. *J. Neurophysiol.* 1997; 77: 2164-74.

28. Kleinert HE, Kutz JE, Atasoy E, Stormo A. Primary repair of flexor tendons. *Orthop. Clin. North Am.* 1973; 4: 865-76.

29. Gallese V, Fadiga L, Fogassi L, Rizzolatti G. Action recognition in the premotor cortex. *Brain* 1996; 119: 593-609.

30. Binkofski F, Buccino G, Stephan KM *et al*. A parieto-premotor network for object manipulation: evidence from neuroimaging. *Exp. Brain Res.* 1999; 128: 210-3.

31. Buccino G, Binkofski F, Riggio L. The mirror neuron system and action recognition. *Brain Lang.* 2004; 89: 370-6.

32. Friston K. Beyond phrenology: what can neuroimaging tell us about distributed circuitry? *Annu. Rev. Neurosci.* 2002; 25: 221-50.

33. Binkofski F, Fink GR, Geyer S *et al*. Neural activity in human primary motor cortex areas 4a and 4p is modulated differentially by attention to action. *J. Neurophysiol.* 2002; 88: 514-9.

34. de Jong BM, Frackowiak RS, Willemsen AT, Paans AM. The distribution of cerebral activity related to visuomotor coordination indicating perceptual and executional specialization. *Brain Res. Cogn. Brain Res.* 1999; 8: 45-59.

35. Flanders M. Functional somatotopy in sensorimotor cortex. *Neuroreport* 2005; 16: 313-6.

36. Schieber MH. Constraints on somatotopic organization in the primary motor cortex. *J. Neurophysiol.* 2001; 86: 2125-43.

37. Boecker H, Lee A, Muhlau M *et al*. Force level independent representations of predictive grip force-load force coupling: a PET activation study. *Neuroimage* 2005; 25: 243-52.

38. Pope P, Wing AM, Praamstra P, Miall RC. Force related activations in rhythmic sequence production. *Neuroimage* 2005; 27: 909-18.

39. Ehrsson HH, Fagergren A, Jonsson T *et al*. Cortical activity in precision- versus power-grip tasks: an fMRI study. *J. Neurophysiol.* 2000; 83: 528-36.

Functional dominance of finger flexion over extension, expressed in left parietal activation